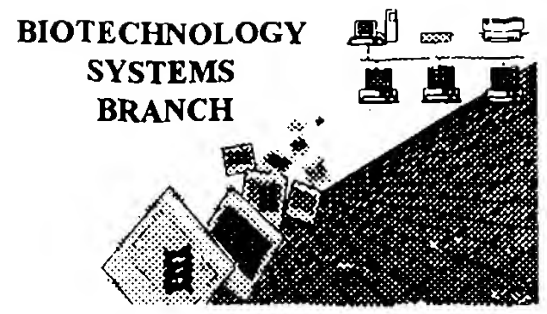

RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 09/643,128
Source: 600
Date Processed by STIC: 11/21/03

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

1) **INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
2) **TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 703-308-4212; FAX: 703-308-4221
Effective 12/13/03: **TELEPHONE: 571-272-2510; FAX: 571-273-0221**

TO **REDUCE** ERRORED SEQUENCE LISTINGS, **PLEASE** USE THE **CHECKER VERSION 4.1 PROGRAM**, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

http://www.uspto.gov/web/offices/pac/checker/chkr41note.htm

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<**http://www.uspto.gov/ebc/efs/downloads/documents.htm**> , **EFS Submission User Manual** - ePAVE)
2. **U.S. Postal Service:** Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. **Hand Carry directly to (EFFECTIVE 12/01/03):**
   U.S. Patent and Trademark Office, Box Sequence, Customer Window, Lobby, Room 1B03, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202
4. **Federal Express, United Parcel Service, or other delivery service to:** U.S. Patent and Trademark Office, Box Sequence, Room 1B03-Mailroom, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202

Revised 10/08/03

Raw Sequence Listing Error Summary

ERROR DETECTED	SUGGESTED CORRECTION	SERIAL NUMBER: 09/643,128

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

1	Wrapped Nucleics Wrapped Aminos	The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."
2	Invalid Line Length	The rules require that a line **not exceed** 72 characters in length. This includes white spaces.
3	Misaligned Amino Numbering	The numbering under each 5th amino acid is misaligned. Do **not** use tab codes between numbers; use **space characters**, instead.
4	Non-ASCII	The submitted file was **not** saved in ASCII(DOS) text, as **required** by the Sequence Rules. **Please ensure your subsequent submission is saved in ASCII text.**
5	Variable Length	Sequence(s)____contain n's or Xaa's representing more than one residue. **Per Sequence Rules, each n or Xaa can only represent a single residue.** Please present the **maximum** number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.
6	PatentIn 2.0 "bug"	A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) _____. Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. **This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.**
7	Skipped Sequences (OLD RULES)	Sequence(s) ____ missing. If intentional, please insert the following lines for **each** skipped sequence (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading) (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) This sequence is intentionally skipped Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to **include** the skipped sequences.
8	Skipped Sequences (NEW RULES)	Sequence(s) _____ missing. If **intentional**, please insert the following lines for **each** skipped sequence. <210> sequence id number <400> sequence id number 000
9	Use of n's or Xaa's (NEW RULES)	Use of **n's** and/or **Xaa's** have been detected in the Sequence Listing. Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of **n** or **Xaa**, and which residue **n** or **Xaa** represents.
10	Invalid <213> Response	Per 1.823 of Sequence Rules, the only **valid** <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is **required** when <213> response is Unknown or is Artificial Sequence
11	Use of <220>	Sequence(s) _____ missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section. (See "Federal Register," 07/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)
12	PatentIn 2.0 "bug"	Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.
13	Misuse of n/Xaa	"n" can **only** represent a single nucleotide; "Xaa" can **only** represent a single amino acid

IFW16

RAW SEQUENCE LISTING DATE: 11/21/2003
PATENT APPLICATION: **US/09/643,128** TIME: 11:01:32

Input Set : **A:\PTO.YF.txt**
Output Set: **N:\CRF4\11212003\I643128.raw**

4 <110> APPLICANT: Jifan Hu, GMR Epigenetics Corporation;
5 Andrew R. Hoffman, Stanford University
7 <120> TITLE OF INVENTION: Gene Inactivation by Targeted DNA Methylation
9 <130> FILE REFERENCE: 10853-005-999
C--> 11 **<140> CURRENT APPLICATION NUMBER: US/09/643,128**
12 <141> CURRENT FILING DATE: 2000-08-21
14 <150> PRIOR APPLICATION NUMBER: US60/96,749
15 <151> PRIOR FILING DATE: 2000-04-12
17 <160> NUMBER OF SEQ ID NOS: 56
19 <170> SOFTWARE: PatentIn For Windows v. 3

Global error.
Consult Sequence Rules.
Consult sample Sequence Listing (attached)

ERRORED SEQUENCES

21 <210> SEQ ID NO: 1
22 <211> LENGTH: 5
23 <212> TYPE: DNA
24 <213> ORGANISM: Artificial sequence
W--> 26 **<220> FEATURE: Hairpin** this belongs on <2237 line. Never insert a response to <2207. It is a "header" only.
W--> 27 **<221> NAME/KEY: m5C**
28 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG
29 dinucleotide sequence
31 <400> SEQUENCE: 1
E--> 32 **m5cgtm5cg**
36 <210> SEQ ID NO: 2
37 <211> LENGTH: 5
38 <212> TYPE: DNA
39 <213> ORGANISM: Artificial sequence
W--> 41 **<220> FEATURE: Hairpin**
W--> 42 **<221> NAME/KEY: m5C**
43 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG
44 dinucleotide sequence
46 <400> SEQUENCE: 2
E--> 47 **m5cgtm5cg**
51 <210> SEQ ID NO: 3
52 <211> LENGTH: 10
53 <212> TYPE: DNA
54 <213> ORGANISM: Artificial sequence
W--> 56 **<220> FEATURE: Hairpin**
W--> 57 **<221> NAME/KEY: m5C**
58 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG

pg 1-5

delete "m5" - show nucleotide only

"n" needs explanation in <2207-<2237 section.
(see item 9 on Error Summary Sheet)

Same error

59 dinucleotide sequence
61 <400> SEQUENCE: 3

RAW SEQUENCE LISTING DATE: 11/21/2003
PATENT APPLICATION: US/09/643,128 TIME: 11:01:32

Input Set : A:\PTO.YF.txt
Output Set: N:\CRF4\11212003\I643128.raw

do not show daster

E--> 62 cgacgtm5cgtm5cg
66 <210> SEQ ID NO: 4
67 <211> LENGTH: 22
68 <212> TYPE: DNA
69 <213> ORGANISM: Artificial sequence
W--> 71 <220> FEATURE: Hairpin
W--> 72 <221> NAME/KEY: m5C
73 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG
74 dinucleotide sequence
76 <300> PUBLICATION INFORMATION:
77 <301> AUTHORs: Xiaoming Yao, Ji-Fan Hu, Mark Daniels, Hadas Shiran, Xiangjun Zhou, Huifan
78 Yan,
79 Hongqi Lu, Zhilan Zeng, Qingxue Wang, Tao Li, and Andrew R. Hoffman
80 <302> TITLE: A methylated oligonucleotide inhibits IGF2 expression and enhances
81 survival
82 in a model of hepatocellular carcinoma
83 <303> JOURNAL: Journal of Clinical Investigation
W--> 84 <307> DATE: in press
86 <400> SEQUENCE: 4
E--> 87 agccm5cgggm5ctgggaggagtm5cgg
91 <210> SEQ ID NO: 5
92 <211> LENGTH: 33
93 <212> TYPE: DNA
94 <213> ORGANISM: Artificial sequence
W--> 96 <220> FEATURE: Hairpin
W--> 97 <221> NAME/KEY: m5C
98 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG
99 dinucleotide sequence
101 <300> PUBLICATION INFORMATION:
102 <301> AUTHORs: Xiaoming Yao, Ji-Fan Hu, Mark Daniels, Hadas Shiran, Xiangjun Zhou, Huifan
103 Yan,
104 Hongqi Lu, Zhilan Zeng, Qingxue Wang, Tao Li, and Andrew R. Hoffman
105 <302> TITLE: A methylated oligonucleotide inhibits IGF2 expression and enhances
106 survival
107 in a model of hepatocellular carcinoma
108 <303> JOURNAL: Journal of Clinical Investigation
W--> 109 <307> DATE: in press
111 <400> SEQUENCE: 6
E--> 112 cgacgtm5cgtm5cgagccm5cgggm5ctgggaggagtm5cgg
116 <210> SEQ ID NO: 6
117 <211> LENGTH: 22
118 <212> TYPE: DNA
119 <213> ORGANISM: Artificial sequence
121 <220> FEATURE:
W--> 122 <221> NAME/KEY:
123 <223> OTHER INFORMATION: Phosphothioate oligonucleotide
125 <300> PUBLICATION INFORMATION:
126 <301> AUTHORs: Xiaoming Yao, Ji-Fan Hu, Mark Daniels, Hadas Shiran, Xiangjun Zhou, Huifan

group all nucleotides into 10's, with a space between each group

22← insert cumulative base total at right margin of each line

group into 10's

33←

127 Yan,

RAW SEQUENCE LISTING DATE: 11/21/2003
PATENT APPLICATION: **US/09/643,128** TIME: 11:01:32

Input Set : **A:\PTO.YF.txt**
Output Set: **N:\CRF4\11212003\I643128.raw**

```
     128       Hongqi Lu, Zhilan Zeng, Qingxue Wang, Tao Li, and Andrew R. Hoffman
     129 <302> TITLE: A methylated oligonucleotide inhibits IGF2 expression and enhances
     130       survival
     131       in a model of hepatocellular carcinoma
     132 <303> JOURNAL: Journal of Clinical Investigation
W--> 133 <307> DATE: in press
     135 <400> SEQUENCE: 6
E--> 136 ggtcacggtcaggcgtagatgg
     140 <210> SEQ ID NO: 7
     141 <211> LENGTH: 21
     142 <212> TYPE: DNA
     143 <213> ORGANISM: Artificial sequence,
W--> 145 <220> FEATURE: Hairpin
W--> 146 <221> NAME/KEY: m5C
     147 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-
methylcytidine (m5C) at CpG
     148       dinucleotide sequence
     150 <400> SEQUENCE: 7
E--> 151 tm5cgctaatctcm5cgcccacm5cgg
     154 <210> SEQ ID NO: 8
     155 <211> LENGTH: 20
     156 <212> TYPE: DNA
     157 <213> ORGANISM: Artificial sequence,
W--> 159 <220> FEATURE: Hairpin
W--> 160 <221> NAME/KEY: m5C
     161 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-
methylcytidine (m5C) at CpG
     162       dinucleotide sequence
     164 <400> SEQUENCE: 8
E--> 165 acm5cggcccttttataatgm5cga
     169 <210> SEQ ID NO: 9
     170 <211> LENGTH: 20
     171 <212> TYPE: DNA
     172 <213> ORGANISM: Artificial sequence,
W--> 174 <220> FEATURE: Hairpin
W--> 175 <221> NAME/KEY: m5C
     176 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-
methylcytidine (m5C) at CpG
     177       dinucleotide sequence
     179 <400> SEQUENCE: 9
E--> 180 tcm5cgcccacm5cggcccttat
     184 <210> SEQ ID NO: 10
     185 <211> LENGTH: 18
     186 <212> TYPE: DNA
     187 <213> ORGANISM: Artificial sequence,
W--> 189 <220> FEATURE: Hairpin
W--> 190 <221> NAME/KEY: m5C
     191 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-
methylcytidine (m5C) at CpG
     192       dinucleotide sequence
     194 <400> SEQUENCE: 10
E--> 195 cam5cgtagccm5cgagagm5ctg
     199 <210> SEQ ID NO: 11
```

group into 10's
22 ← insert
c-myc
this goes on <2237 here.
Do not insert explanation on <2137 line.
Hairpin
m5C
group into 10's
21 ←
c-myc
Hairpin
m5C
group into 10's
20 ←
c-myc
10's
20 ←
HIV
Hairpin
m5C
10's
18 ←
FYI
IMPORTANT

<110> Smith, John; Smithgene Inc.

<120> Example of a Sequence Listing

<130> 01-00001

<140> PCT/EP98/00001
<141> 1998-12-31

<150> US 08/999,999
<151> 1997-10-15

<160> 4

<170> PatentIn version 2.0

<210> 1
<211> 389
<212> DNA
<213> Paramecium sp.

<220>
<221> CDS
<222> (279)...(389)

<300>
<301> Doe, Richard
<302> Isolation and Characterization of a Gene Encoding a Protease from Paramecium sp
<303> Journal of Genes
<304> 1
<305> 4
<306> 1-7
<307> 1988-06-31
<308> 123456
<309> 1988-06-31

<400> 1

agctgtagtc attcctgtgt cctcttctct ctgggcttct cacccctgct atcagatctc 60

agggagagtg tcttgaccct cctctgcctt tgcagcttca caggcaggca ggcaggcagc 120

tgatgtggca attgctggca gtgccacagg ctttttagcc aggcttaggg tgggttccgt 180

cgcggcgcgg cggccccttt cgcgctcctc tcgcgccttt ctctcgcttt cctctcgctc 240

```
                                                                atg  gtt  tca  atg  ttc  agc   290
                                                                Met  Val  Ser  Met  Phe  Ser
                                                                 1                   5

ttg  tct  ttc  aaa  tgg  cct  gga  ttt  tgt  ttg  btt  gtt  tgt  ttg  ttc  caa   342
Leu  Ser  Phe  Lys  Trp  Pro  Gly  Phe  Cys  Leu  Phe  Val  Cys  Leu  Phe  Gln
               10                        15                  20

tgt  ccc  aaa  gtc  ctc  ccc  tgt  cac  tca  tca  ctg  cag  ccg  aat  ctt        389
Cys  Pro  Lys  Val  Leu  Pro  Cys  His  Ser  Ser  Leu  Gln  Pro  Asn  Leu
          25                        30                  35
```

<210> 2
<211> 37
<212> PRT
<213> Paramecium sp.

<400> 2

```
Met  Val  Ser  Met  Phe  Ser  Leu  Ser  Phe  Lys  Trp  Pro  Gly  Phe  Cys  Leu
 1               5                        10                  15

Phe  Val  Cys  Leu  Phe  Gln  Cys  Pro  Lys  Val  Leu  Pro  Cys  His  Ser  Ser
            20                        25                  30

Leu  Gln  Pro  Asn  Leu
          35
```

<210> 3
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed peptide based on size and polarity to act as a linker between the alpha and beta chains of Protein XYZ

<400> 3

```
Met  Val  Asn  Leu  Glu  Pro  Met  His  Thr  Glu  Ile
 1               5                        10
```

<210> 4
<400> 4
000

[Annex VIII follows]

identifiers and their accompanying information as shown in the following table. The numeric identifier shall be used only in the "Sequence Listing." The order and presentation of the items of information in the "Sequence Listing" shall conform to the arrangement given below. Each item of information shall begin on a new line and shall begin with the numeric identifier enclosed in angle brackets as shown. The submission of those items of information designated with an "M" is mandatory. The submission of those items of information designated with an "O" is optional. Numeric identifiers <110> through <170> shall only be set forth at the beginning of the "Sequence Listing." The following table illustrates the numeric identifiers.

Numeric Identifier	Definition	Comments and Format	Mandatory (M) or Optional (O)
<110>	Applicant	Preferably max. of 10 names; one name per line; preferable format: Surname, Other Names and/or Initials	M
<120>	Title of Invention		M
<130>	File Reference	Personal file reference	M, when filed prior to assignment of appl. number
<140>	Current Application Number	Specify as: US 07/999,999 or PCT/US96/99999	M, if available
<141>	Current Filing Date	Specify as: yyyy-mm-dd	M, if available
<150>	Prior Application Number	Specify as: US 07/999,999 or PCT/US96/99999	M, if applicable include priority documents under 35 USC 119 and 120
<151>	Prior Application Filing Date	Specify as: yyyy-mm-dd	M, if applicable
<160>	Number of SEQ ID NOs	Count includes total number of SEQ ID NOs	M
<170>	Software	Name of software used to create the Sequence Listing	O
<210>	SEQ ID NO:#:	Response shall be an integer representing the SEQ ID NO shown	M
<211>	Length	Respond with an integer expressing the number of bases or amino acid residues	M

<212>	Type	Whether presented sequence molecule is DNA, RNA, or PRT (protein). If a nucleotide sequence contains both DNA and RNA fragments, the type shall be "DNA." In addition, the combined DNA/RNA molecule shall be further described in the <220> to <223> feature section.	M
<213>	Organism	Scientific name, i.e. Genus/species, Unknown or Artificial Sequence. In addition, the "Unknown" or "Artificial Sequence" organisms shall be further described in the <220> to <223> feature section.	M
<220>	Feature	Leave blank after <220>. <221-223> provide for a description of points of biological significance in the sequence.	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence; if ORGANISM is "Artificial Sequence" or "Unknown" molecule is combined DNA/RNA.
<221>	Name/Key	Provide appropriate identifier for feature, preferably from WIPO Standard ST.25 (1998), Appendix 2, Tables 5 and 6	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence
<222>	Location	Specify location within sequence; where appropriate state number of first and last bases/amino acids	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified

		in feature	base was used in a sequence
<223>	Other Information	Other relevant information; four lines maximum	H, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence; if ORGANISM is "Artificial Sequence" or "Unknown"; if molecule is combined DNA/RNA.
<300>	Publication Information	Leave blank after <300>	O
<301>	Authors	Preferably max of ten named authors of publication; specify one name per line; preferable format: Surname, Other Names and/or Initials	O
<302>	Title		O
<303>	Journal		O
<304>	Volume		O
<305>	Issue		O
<306>	Pages		O
<307>	Date	Journal date on which data published; specify as yyyy-mm-dd, mm-yyyy or Season-yyyy	O
<308>	Database Accession Number	Accession number assigned by database including database name	O
<309>	Database Entry Date	Date of entry in database; specify as yyyy-mm-dd or mm-yyyy	O
<310>	Patent Document Number	Document number; for patent-type citations only. Specify as, for example, US 07/999,999	O

<311>	Patent Filing Date	Document filing date, for patent-type citations only; specify as yyyy-mm-dd	O
<312>	Publication Date	Document publication date, for patent-type citations only; specify as yyyy-mm-dd	O
<313>	Relevant Residues	FROM (position) TO (position)	O
<400>	Sequence	SEQ ID NO should follow the numeric identifier and should appear on the line preceding the actual sequence	M

5. Section 1.824 is revised to read as follows:

1.824 Form and format for nucleotide and/or amino acid sequence submissions in computer readable form.

(a) The computer readable form required by 1.821(c) shall meet the following specifications:

(1) The computer readable form shall contain a single "Sequence Listing" as either a diskette, series of diskettes, or other permissible media outlined in paragraph (c) of this section.

(2) The "Sequence Listing" in paragraph (a) (1) of this section shall be submitted in American Standard Code for Information Interchange (ASCII) text. No other formats shall be allowed.

(3) The computer readable form may be created by any means, such as word processors, nucleotide/amino acid sequence editors or other custom computer programs; however, it shall conform to all specifications detailed in this section.

(4) File compression is acceptable when using diskette media, so long as the compressed file is in a self-extracting format that will decompress on one of the systems described in paragraph (b) of this section.

(5) Page numbering shall not appear within the computer readable form version of the "Sequence Listing" file.

(6) All computer-readable forms shall have a label permanently affixed thereto on which has been hand-printed or typed: the name of the applicant, the title of the invention, the date on which the data were recorded on the computer readable form, the operating system used, a reference number, and an application serial number and filing date, if known.

(b) Computer readable form submissions must meet these format requirements:

(1) Computer: IBM PC/XT/AT, or compatibles, or Apple Macintosh;

(2) Operating System: MS-DOS, Unix or Macintosh;